

Control of the repetitive firing in the squid giant axon using electrical fields

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Abstract

In this research, the aim is to develop a repetitive firing stopper mechanism using electrical fields exerted on the fiber. The Hodgkin – Huxley nerve fiber model is used for modeling the membrane potential behavior. The repetitive firing of the nerve fiber can be stopped using approaches based on the control theory where the nonlinear Hodgkin – Huxley model is used to achieve this goal. The effects of the electrical field are considered as an additive quantity over the equilibrium potentials of the cell membrane channels

Keywords: Squid Giant Axon, Hodgkin - Huxley Model, Electrical Field Stimulation, Bifurcation, Washout Filter, Projective Control

1 Introduction

The repetitive firing of the nerve fibers in the living beings is an important subject of the biophysical research since the phenomenon has various meanings. It may have a role in several diseases like epilepsy [Pellock et.al (2001)] but have also a role in the formation of heart beats where the oscillation frequency is in fact represents the heart rate. The Hodgkin – Huxley nerve fiber model [Hodgkin et.al (1952)] provides a very useful framework for simulation based neurophysiologic studies where the variation of the membrane potential is modeled basically as a fourth order nonlinear differential equation. The basic model in [Hodgkin et.al (1952)] allows the external current injection as the system input whereas an additional cell membrane potential can also be considered as an input which is the case in [Wang et.al. (2004)]. The electrical fields around the nerve cell membranes can induce small electric potentials which may lead to different behaviors as stated in [Wang et.al. (2004), Kotnik et.al (1998)] however the potential induction mechanism can also be used as a repetitive firing control mechanism which is the main point of this research. The repetitive firing condition on the Hodgkin – Huxley nerve fiber model is detected using a bifurcation discovery tool like MATCONT [Dhooge et.al. (2003)] and the washout filter [Hassounieh et.al. (2004), Wang et.al. (2000)] and projective control [Medanic

(1978)] is integrated to derive a membrane additive voltage profile. This voltage profile is converted into an electrical field requirement profile using an approach derived from [Kotnik et.al. (1998)]. Using electrical energy in treatment of neurological disorders is a wide part of neurophysiology research where one of the most prominent applications is the deep brain stimulation which is used in the treatment of Parkinson's disease [Moro et.al. (2006)] and depression [Mayberg et.al. (2005)]. The mechanism is that a device implanted in the brain tissue sending electrical pulses to the brain. This can be taught as a current injection system whereas in this research the mechanism of electric field induction is used to obtain a response from the neurological tissue. The research can be a base point for further advancements in electrical field stimulation of the central nervous system. Using electrical energy in treatment of neurological disorders is a wide part of neurophysiology research where one of the most prominent applications is the deep brain stimulation which is used in the treatment of Parkinson's disease [Moro et.al. (2006)] and depression [Mayberg et.al. (2005)]. The mechanism is that a device implanted in the brain tissue sending electrical pulses to the brain. This can be taught as a current injection system whereas in this research the mechanism of electric field induction is used to obtain a response from the neurological tissue. The research can be a base point for further advancements in electrical field stimulation of the central nervous system. In this paper, first of all the Hodgkin – Huxley model of nerve fibers together with the electrical field effects are reviewed and then the methods of projective control theory and washout filters are presented. Next the approach of this research is described in detail.

2 Materials and Methods

2.1 Hodgkin Huxley Model and Electrical Field Interaction

Hodgkin – Huxley model nerve fiber dynamics [Hodgkin et.al. (1952)] is a fourth order differential equation derived for modeling the behavior of the membrane potential as shown below:

$$C_m \frac{dV}{dt} = -g_{Na} m^3 h (V - V_{Na}) - g_K n^4 (V - V_K) - g_L (V - V_L) + I_{ext} \quad (2.1)$$

$$\frac{dn}{dt} = \alpha_n (1 - n) - \beta_n n$$

$$\frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m$$

$$\frac{dh}{dt} = \alpha_h (1 - h) - \beta_h h$$

$$\alpha_n = \frac{0.1 - 0.01V}{\exp(1 - 0.1V) - 1}, \beta_n = 0.125 \exp\left(-\frac{V}{80}\right)$$

$$\alpha_m = \frac{2.5 - 0.1V}{\exp(2.5 - 0.1V) - 1}, \beta_m = 4\exp\left(-\frac{V}{18}\right)$$

$$\alpha_h = 0.07\exp\left(-\frac{V}{20}\right), \beta_h = \frac{1}{\exp(3 - 0.1V) - 1}$$

The definitions of the parameters are:

V : the displacement of the cell membrane potential from its resting value in mV

n : is a dimensional variable which can vary between 0 and 1 representing the proportion of activating molecules of the potassium channel

m : same type of variable as n which represents the proportion of the activating molecules of the sodium channel

h : same type of variable as n which represents the proportion of the inactivating molecules of the sodium channel

I_{ext} : external current injection in $\frac{\mu A}{cm^2}$

g_{Na} : sodium channel conductance in $\frac{mS}{cm^2}$

g_K : potassium channel conductance in $\frac{mS}{cm^2}$

g_L : leakage conductance in $\frac{mS}{cm^2}$ due to the chloride and other ions which leads to a leaking current flow. Because of that the behaviour is modeled as a conductance.

C_m : membrane capacitance in $\frac{\mu F}{cm^2}$

V_{Na} : sodium channel resting potential in mV

V_K : potassium channel resting potential in mV

V_L : the level of potential where the leakage current reduces to zero

In the experimentation performed by Alan Hodgkin and his colleagues the nominal values determined are:

$$g_{Na} = 36 \frac{mS}{cm^2} \tag{2.2}$$

$$g_K = 120 \frac{mS}{cm^2}$$

$$g_L = 0.3 \frac{mS}{cm^2}$$

$$V_K = -12mV$$

$$V_{Na} = 115mV$$

$$V_L = 10.613mV$$

$$C_m = 0.91 \frac{\mu F}{cm^2}$$

In this work the external current injection is set to zero by default. It is to be used as an external stimulus for stabilizing the neuron with the washout filter. The external effect input to the model in our case is the external voltage induction on the cell membrane by the electric fields which is added to (2.1) as:

$$\begin{aligned}
C_m \frac{dV}{dt} &= -g_{Na} m^3 h (V + V_E - V_{Na}) - g_K n^4 (V + V_E - V_K) - g_L (V + V_E - V_L) + I_{ext} \\
\frac{dn}{dt} &= \alpha_n (1 - n) - \beta_n n \\
\frac{dm}{dt} &= \alpha_m (1 - m) - \beta_m m \\
\frac{dh}{dt} &= \alpha_h (1 - h) - \beta_h h \\
\alpha_n &= \frac{0.1 - 0.01V}{\exp(1 - 0.1V) - 1}, \beta_n = 0.125 \exp\left(-\frac{V}{80}\right) \\
\alpha_m &= \frac{2.5 - 0.1V}{\exp(2.5 - 0.1V) - 1}, \beta_m = 4 \exp\left(-\frac{V}{18}\right) \\
\alpha_h &= 0.07 \exp\left(-\frac{V}{20}\right), \beta_h = \frac{1}{\exp(3 - 0.1V) - 1}
\end{aligned}
\tag{2.3}$$

The term V_E is the potential induced on the cell membrane by any external effect which is the electrical field in this case. If this is due to a time varying electrical field relationship between V_E and the exerting electrical field E is obtained from the solution of Laplace's partial differential equation which is used by [Kotnik, 1998] to obtain the following:

$$V_E = F(s) E(s) R \cos(\theta) \tag{2.4}$$

where $E(s)$ is the electrical field time course defined in the Laplace domain, R is the radius of the cell soma and θ is the directional angle of the electrical field exerted upon the nerve fibers. Finally $F(s)$ is the transfer function defined as:

$$F(s) = \frac{a_1 s^2 + a_2 s + a_3}{b_1 s^2 + b_2 s + b_3} \tag{2.5}$$

with its coefficients:

$$\begin{aligned}
a_1 &= 3d\lambda_o (\lambda_i (3R^2 - 3dR + d^2) + \lambda_m (3dR - d^2)) \\
a_2 &= 3d ((\lambda_i \varepsilon_o + \lambda_o \varepsilon_i) (3R^2 - 3dR + d^2) + (\lambda_m \varepsilon_o + \lambda_o \varepsilon_m) (3dR - d^2)) \\
a_3 &= 3d\varepsilon_o (\varepsilon_i (3R^2 - 3dR + d^2) + \varepsilon_m (3dR - d^2)) \\
b_1 &= 2R^3 (\lambda_m + 2\lambda_o) (\lambda_m + \frac{1}{2}\lambda_i) + 2(R - d)^3 (\lambda_m - \lambda_o) (\lambda_i - \lambda_m) \\
b_2 &= 2R^3 (\lambda_i (\frac{1}{2}\varepsilon_m + \varepsilon_o) + \lambda_m (\frac{1}{2}\varepsilon_i + 2\varepsilon_m + 2\varepsilon_o) + \lambda_o (\varepsilon_i + 2\varepsilon_m)) + 2(R - d)^3 \\
&\quad \times (\lambda_i (\varepsilon_m - \varepsilon_o) + \lambda_m (\varepsilon_i - 2\varepsilon_m + \varepsilon_o) - \lambda_o (\varepsilon_i - \varepsilon_m)) \\
b_3 &= 2R^3 (\varepsilon_m + 2\varepsilon_o) (\varepsilon_m + \frac{1}{2}\varepsilon_i) + 2(R - d)^3 (\varepsilon_m - \varepsilon_o) (\varepsilon_i - \varepsilon_m)
\end{aligned}
\tag{2.6}$$

The parameters of (2.6) are defined in the following table in reference to [Kotnik, 1998]:

Table 1: The values of electrical parameters for the considered cell membrane (values are from Kotnik et.al)

Parameter	Definition	Value
λ_i	Cytoplasmic conductivity	$0.3 \text{ S} \cdot \text{m}^{-1}$
ε_i	Cytoplasmic permittivity	$7.1 \cdot 10^{-10} \text{ A} \cdot \text{s} \cdot \text{V}^{-1} \cdot \text{m}^{-1}$
λ_m	Membrane conductivity	$3 \cdot 10^{-7} \text{ S} \cdot \text{m}^{-1}$
ε_m	Membrane permittivity	$4.4 \cdot 10^{-11} \text{ A} \cdot \text{s} \cdot \text{V}^{-1} \cdot \text{m}^{-1}$
λ_o	Extracellular medium conductivity	$3 \cdot 10^{-1} \text{ S} \cdot \text{m}^{-1}$
ε_o	Extracellular medium permittivity	$7.1 \cdot 10^{-10} \text{ A} \cdot \text{s} \cdot \text{V}^{-1} \cdot \text{m}^{-1}$
R	Cell soma radius	$10 \mu\text{m}$
d	Membrane thickness	5 nm

The relation in (2.4) is derived using admittivity operators. The details of derivations are given in the relevant research [Kotnik et.al. (1998)]. In order to obtain the level of electric field required for the intended operation the following can be derived:

$$E(s) = \frac{1}{R \cos(\theta)} \Phi(s) V_E \quad (2.7)$$

where,

$$\Phi(s) = \frac{b_1 s^2 + b_2 s + b_3}{a_1 s^2 + a_2 s + a_3} \quad (2.8)$$

The above can be written since the order of the numerator and denominator in (2.5) is same where the inversion does not change the properness of the function. For maximum efficiency the directional angle of the field θ should be zero.

2.2 Projective Control Theory

The projective control approach is a linear control methodology that derives an output feedback controller from a full state feedback design. The transformation from the full state feedback to the output feedback is performed through the orthogonal projection which operates on the closed loop eigenspectrum of the full state feedback design. Before going into the detail of the projective control approach a review of full state feedback control approach is given for convenience. Consider a linear system depicted by:

$$\dot{\mathbf{x}} = \mathbf{A}\mathbf{x} + \mathbf{B}\mathbf{u} \quad (2.9)$$

where

$$\mathbf{x} \in \mathbb{R}^n, \mathbf{u} \in \mathbb{R}^m, \mathbf{A} \in \mathbb{R}^{n \times n}, \mathbf{B} \in \mathbb{R}^{n \times m}$$

If one designs a full state feedback controller as

$$\mathbf{u} = -\mathbf{K}\mathbf{x}$$

the closed loop dynamics is now

$$\dot{\mathbf{x}} = (\mathbf{A} - \mathbf{BK}) \mathbf{x}$$

The eigenspectrum of this closed loop dynamics is defined by the equation shown below:

$$(\mathbf{A} - \mathbf{BK}) \mathbf{V} = \mathbf{V}\Lambda \quad (2.10)$$

where Λ is the diagonal matrix with the entries of eigenvalues of the closed loop dynamics (or the eigenvalues of $\mathbf{A} - \mathbf{BK}$) and is the matrix of the corresponding eigenvectors. If one is thinking of making a static output feedback from $\mathbf{y} = \mathbf{C}\mathbf{x}$ ($\mathbf{C} \in \mathbb{R}^{q \times n}$, $\mathbf{y} \in \mathbb{R}^q$) as $\mathbf{u} = -\mathbf{K}_o\mathbf{y} = -\mathbf{K}_o\mathbf{C}\mathbf{x}$. If this feedback is assumed to retain q eigenvalues out of Λ (denote this as Λ_q and corresponding eigenvectors from V as V_q) the following should also be written:

$$(\mathbf{A} - \mathbf{BK}_o\mathbf{C}) \mathbf{V}_q = \mathbf{V}_q\Lambda_q \quad (2.11)$$

Combining (2.10) and (2.11) the following can be written:

$$(\mathbf{A} - \mathbf{BK}) \mathbf{V} = (\mathbf{A} - \mathbf{BK}_o\mathbf{C}) \mathbf{V}_q$$

This allows one to solve for

$$\mathbf{K}_o$$

as:

$$\mathbf{K}_o = \mathbf{K}\mathbf{V}_q (\mathbf{C}\mathbf{V}_q)^{-1} \quad (2.12)$$

For the nonlinear systems the model should be linearized using the Jacobian (or the Taylor series).

2.3 Linearization and Bifurcation

As it is just stated the projective control approach requires linearization of the nonlinear model. For the case of a standard nonlinear system representation like $\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x}, \mathbf{u})$ the following equations are written:

$$\begin{aligned} \dot{\mathbf{x}} &= \mathbf{A}\mathbf{x} + \mathbf{B}\mathbf{u} + \mathbf{H}(\mathbf{x}, \mathbf{u}) \\ \mathbf{A} &= \left. \frac{\partial \mathbf{f}}{\partial \mathbf{x}} \right|_{\mathbf{x}=\mathbf{x}_0} \\ \mathbf{B} &= \left. \frac{\partial \mathbf{f}}{\partial \mathbf{u}} \right|_{\mathbf{u}=\mathbf{u}_0} \end{aligned} \quad (2.13)$$

where $\mathbf{x} \in \mathbb{R}^n$ is the state of the system, $\mathbf{u} \in \mathbb{R}^m$ is the input and $\mathbf{H}(\mathbf{x}, \mathbf{u})$ is the higher order nonlinear terms and \mathbf{x}_0 is the equilibrium point. The eigenvalues of the matrix characterizes the stability of \mathbf{x}_0 . If the instability of the system (2.13) is due to a single pair of complex conjugate eigenvalues the resultant event is called as Hopf bifurcation. On the other hand if there is a pair of eigenvalues with the same values and opposite signs the resultant issue is called as the saddle node bifurcation. For the Hodgkin – Huxley model the repetitive firing in non – stimulated (current or other external effects) is a result of the bifurcation phenomenon. The bifurcation characteristics of the system can be changed by using specially designed controllers. However, many of the controllers lead to a change in the position of the equilibrium point. This is not a problem in general but if the equilibrium point should not be changed one has to incorporate a washout filter which blocks the steady state (DC) inputs to the system. The washout filter itself is a linear high – pass filter which can be mathematically defined as shown below:

$$\begin{aligned}\dot{\mathbf{z}} &= \mathbf{A}_w \mathbf{z} + \mathbf{B}_w \xi \\ \psi &= \mathbf{A}_w \mathbf{z} + \mathbf{B}_w \xi\end{aligned}\tag{2.14}$$

where $\mathbf{z} \in \mathbb{R}^p$, $\psi \in \mathbb{R}^p$, $\xi \in \mathbb{R}^p$, $\mathbf{A}_w \in \mathbb{R}^{p \times p}$ and $\mathbf{B}_w \in \mathbb{R}^{p \times p}$

If the above dynamics is expressed in the Laplace domain the following result can be obtained:

$$\mathbf{G}(s) = \frac{\psi(s)}{\xi(s)} = \mathbf{A}_w [s\mathbf{I}_{p \times p} - \mathbf{A}_w]^{-1} \mathbf{B}_w + \mathbf{B}_w\tag{2.15}$$

where $\mathbf{G}(s)$ is the multi – input and multi – output transfer function from the input ξ to output ψ . It is clearly noted that the following limit tends to zero.

$$\lim_{s \rightarrow 0} \mathbf{G}(s) \rightarrow 0\tag{2.16}$$

The above result means that the system in (2.14) blocks the steady state inputs. This property is the core part of the control mechanisms aided with a washout filter.

2.4 Hodgkin – Huxley Model and application

For the Hodgkin – Huxley model in consideration first of all a linearization should be done. So the linearization will lead to the linearized model in (2.9) with the matrix \mathbf{A} as:

$$\mathbf{A} = \left[\begin{array}{cccc} \frac{\partial V}{\partial n} & \frac{\partial V}{\partial n} & \frac{\partial V}{\partial m} & \frac{\partial V}{\partial h} \\ \frac{\partial V}{\partial n} & \frac{\partial V}{\partial n} & 0 & 0 \\ \frac{\partial V}{\partial m} & 0 & \frac{\partial m}{\partial m} & 0 \\ \frac{\partial h}{\partial V} & 0 & 0 & \frac{\partial h}{\partial h} \end{array} \right] \bigg|_{V_E=0}, \mathbf{x} = \begin{bmatrix} V \\ n \\ m \\ h \end{bmatrix}\tag{2.17}$$

$$\begin{aligned}
\frac{\partial \dot{V}}{\partial V} &= \frac{1}{C_m} (-g_{Na} m^3 h - g_K n^4 - g_L) \\
\frac{\partial \dot{V}}{\partial n} &= -\frac{4}{C_m} g_K n^3 (V - V_K) \\
\frac{\partial \dot{V}}{\partial m} &= -\frac{3}{C_m} g_{Na} m^2 h (V - V_{Na}) \\
\frac{\partial \dot{V}}{\partial h} &= -\frac{1}{C_m} g_{Na} m^3 (V - V_{Na})
\end{aligned} \tag{2.18}$$

$$\begin{aligned}
\frac{\partial \dot{n}}{\partial V} &= -1/100 / (\exp(1 - 1/10V) - 1)(1 - n) + \\
&1/10 \times (1/10 - 1/100V) / (\exp(1 - 1/10V) - 1)^2 \times (1 - n) \exp(1 - 1/10V) + 1/640 \times \exp(-1/80V)n \\
\frac{\partial \dot{m}}{\partial V} &= -1/10 / (\exp(5/2 - 1/10V) - 1)(1 - m) + \\
&1/10(5/2 - 1/10V) / (\exp(5/2 - 1/10V) - 1)^2 (1 - m) \times \exp(5/2 - 1/10V) + 2/9 \exp(-1/18V)m \\
\frac{\partial \dot{h}}{\partial V} &= -7/2000 \exp(-1/20V)(1 - h) - 1/10 / (\exp(3 - 1/10V) + 1)^2 h \times \exp(3 - 1/10V) \\
\frac{\partial \dot{n}}{\partial n} &= -(\alpha_n + \beta_n) \\
\frac{\partial \dot{m}}{\partial m} &= -(\alpha_m + \beta_m) \\
\frac{\partial \dot{h}}{\partial h} &= -(\alpha_h + \beta_h)
\end{aligned} \tag{2.19}$$

The terms are given in Section 2.1. The input u and the matrix B is:

$$\mathbf{B} = \begin{bmatrix} \frac{1}{C_m} (-g_{Na} m^3 h - g_K n^4 - g_L) \\ 0 \\ 0 \\ 0 \end{bmatrix}, \mathbf{u} = V_E \tag{2.20}$$

In the next, the repetitive firing condition should be found which is done through bifurcation analysis using the MATCONT toolbox of MATLAB [®]. For this purpose, we will analyze the case where there is a physiological condition on the sodium channel. That is the deviation in the equilibrium (rest) potential of the channel in which MATCONT provides the following data:

In order to continue the application, a washout filter should be proposed. The input of the washout filter should be a measurable variable which is in this case the membrane potential of the nerve fiber. So the washout filter will be of the following form:

$$\begin{aligned}
\dot{z} &= a_w z + b_w V \\
y &= a_w z + b_w V
\end{aligned} \tag{2.21}$$

Table 2: The repetitive firing condition as a result of deviation in the sodium channel

Parameter & Prop	$V_{Na} = 199.134$
Eigenvalues	$\lambda_1 = -5.04011$ $\lambda_2 = -0.1257$ $\lambda_3 = j0.3958$ $\lambda_4 = -j0.3958$
Equilibrium Points	$V = 0.93404938$ $n = 0.33208269$ $m = 0.059059$ $h = 0.5631245$
Type of Bifurcation	Hopf

In order to have a stable filter the condition

$$a_w < 0$$

should be satisfied. For a practical case one can choose $a_w = -0.01$ and $b_w = 1$. The resultant filter is augmented into the linearized nerve model in (2.17) - (2.21) to obtain:

$$\dot{\mathbf{x}}_f = \mathbf{A}_f \mathbf{x}_f + \mathbf{B}_f V_E$$

$$\mathbf{A}_f = \left[\begin{array}{ccccc} \frac{\partial \dot{V}}{\partial n} & \frac{\partial \dot{V}}{\partial n} & \frac{\partial \dot{V}}{\partial m} & \frac{\partial \dot{V}}{\partial h} & 0 \\ \frac{\partial \dot{V}}{\partial n} & \frac{\partial \dot{V}}{\partial n} & 0 & 0 & 0 \\ \frac{\partial \dot{V}}{\partial m} & 0 & \frac{\partial \dot{m}}{\partial m} & 0 & 0 \\ \frac{\partial \dot{h}}{\partial V} & 0 & 0 & \frac{\partial \dot{h}}{\partial h} & 0 \\ \frac{\partial \dot{V}}{\partial V} & 0 & 0 & 0 & a_w \end{array} \right]_{V_E}, \mathbf{B}_f = \begin{bmatrix} \mathbf{B} \\ 0 \end{bmatrix}, \mathbf{x}_f = \begin{bmatrix} V \\ n \\ m \\ h \\ z \end{bmatrix} \quad (2.22)$$

Numerical representation of the above matrix for the values given in the Table 2 is now:

$$\begin{bmatrix} \dot{V} \\ \dot{n} \\ \dot{m} \\ \dot{h} \\ \dot{z} \end{bmatrix} = \begin{bmatrix} -0.8261 & -74.9539 & 154.0073 & 5.3840 & 0 \\ 0.0029 & -0.1850 & 0 & 0 & 0 \\ 0.0278 & 0 & -4.0361 & 0 & 0 \\ -0.0042 & 0 & 0 & -0.1186 & 0 \\ 1 & 0 & 0 & 0 & -0.01 \end{bmatrix} \begin{bmatrix} V \\ n \\ m \\ h \\ z \end{bmatrix} + \begin{bmatrix} -0.8261 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix} V_E \quad (2.23)$$

The output feedback will be taken from the output of the washout filter so the output feedback matrix is $\mathbf{C} = [1 \ 0 \ 0 \ 0 \ -0.01]$. In order to proceed, a full state feedback controller is necessary for the linear system presented in (2.23). This can be obtained using the linear quadratic theory (LQR) and the MATLAB's `lqr(A, B, Q, R)` command directly results a full state feedback coefficient matrix \mathbf{K}_f where $V_E = -\mathbf{K}_f \mathbf{x}$. The obtained gain matrix \mathbf{K}_f minimizes the infinite horizon quadratic gain index shown below:

$$J = \int_0^{\infty} (\mathbf{x}^T \mathbf{Q} \mathbf{x} + \mathbf{u}^T \mathbf{R} \mathbf{u}) dt \quad (2.24)$$

Taking $\mathbf{Q} = q\mathbf{I}_{4 \times 4}$ and $\mathbf{R} = 1$ considering the problem of this research the above index is rewritten as:

$$J = \int_0^{\infty} (q [V^2 + n^2 + m^2 + h^2] + V_E^2) dt \quad (2.25)$$

Substituting $q = 100$ and invoking the necessary command the full state feedback gain coefficient yields:

$$\mathbf{K}_f = [-10.5426 \ 89.5670 \ -133.4628 \ -6.4330 \ -9.8885] \quad (2.26)$$

The closed loop spectrum ($\mathbf{A}_f - \mathbf{B}_f \mathbf{K}_f$) for the new case is:

$$\mathbf{\Lambda}_f = \begin{bmatrix} -8.8641 & 0 & 0 & 0 & 0 \\ 0 & -3.7002 & 0 & 0 & 0 \\ 0 & 0 & -1.0170 & 0 & 0 \\ 0 & 0 & 0 & -0.1849 & 0 \\ 0 & 0 & 0 & 0 & -0.1186 \end{bmatrix} \quad (2.27)$$

And the corresponding eigenvectors are:

$$\mathbf{V}_f = \begin{bmatrix} 0.9937 - 0.9621i & 0.7096 & 0.0253 & 0.0011 \\ -0.0003 & 0.0008 - 0.0024i & 0.9891 & 0.0000 \\ -0.0057 & -0.0796 & 0.0065 & 0.0002 & 0.0000 \\ 0.0005 & -0.0011 & 0.0033 & 0.0016 & -1.0000 \\ -0.1122 & 0.2607 & -0.7046 & -0.1448 & -0.0097 \end{bmatrix} \quad (2.28)$$

The projective control law will make feedback only from the washout filter thus the dimension of the feedback is one and the number of guaranteed retainable eigenvalues is also equal to one. So it is best to retain the eigenvalue farthest from the imaginary axis which is the one at -8.8641 so the matrix

$$\mathbf{V}_q$$

is only a single column vector and found as:

$$\mathbf{V}_q = \begin{bmatrix} 0.99367 \\ -0.00032859 \\ -0.0057199 \\ 0.00048023 \\ -0.11223 \end{bmatrix} \quad (2.29)$$

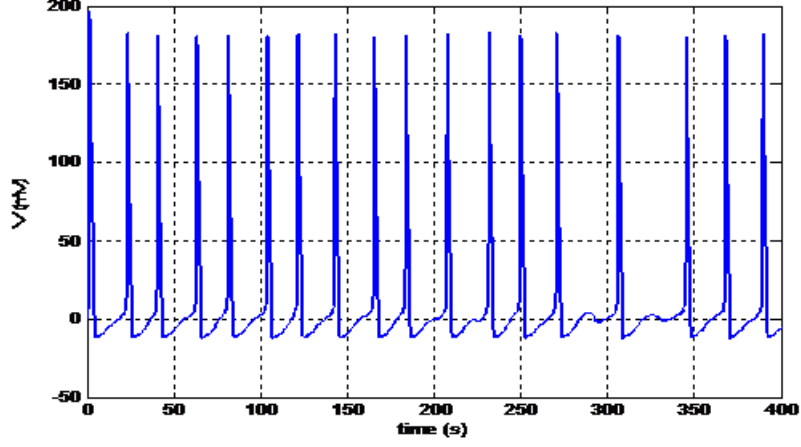


Figure 3.1: The repetitive firing response of the bifurcating nerve fiber

Applying the projection equation in (2.12) gives the feedback gain from the washout filter output:

$$K_o = \mathbf{K}\mathbf{V}_q (\mathbf{C}\mathbf{V}_q)^{-1} = -8.6805 \quad (2.30)$$

And applying the feedback as $\mathbf{A}_f - \mathbf{B}_f K_o \mathbf{C}$ yields the output feedback closed loop eigenvalues:

$$\begin{bmatrix} -8.8641 \\ -3.1436 \\ -0.0013609 \\ -0.21673 \\ -0.12075 \end{bmatrix} \quad (2.31)$$

So the resultant closed loop is a stable system with the expected eigenvalue at -8.8641 in the right place. The control law together with the washout filter is:

$$\begin{aligned} \dot{z} &= -0.01z + V \\ V_E &= -K_o(-0.01z + V) \end{aligned} \quad (2.32)$$

3 Results and Discussion

The uncontrolled nerve fiber model in (2.1) with the parameters in (2.2) except the deviated parameter which is given in Table 2 will yield a repetitive firing action potential as shown in Figure 1:

When the control law of (2.32) is applied through the external voltage input of the model in (2.3) the response of the nerve fiber becomes that of the Figure 2.

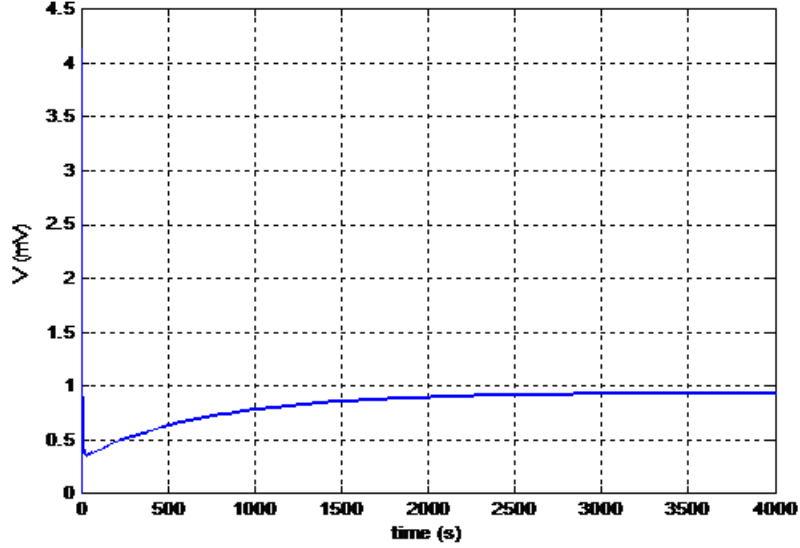


Figure 3.2: The stabilized response of the nerve fiber

The required level of electrical field can be obtained using the inversion system presented in (2.7) with the parameters given in Table 1. Required level of electric field is presented in Figure 3.

As it is expected the level of electric field goes to zero since it stabilized the equilibrium condition on the nerve fiber. The steady state portion of the electric field is not allowed to pass from the washout filter and thus it stays at zero forever after the stabilization. This makes the electric field stimulation of the nerve fiber very short. This is a good advantage because of the fact that the level of electric field required is quite high as seen from Figure 3. In this research, we have presented a stabilization scheme for stopping the repetitive firing of the nerve fiber. In order to achieve the goal, the Hodgkin – Huxley model of the squid giant axon is taken into consideration. A condition on the sodium channel is found where the fiber starts to produce repetitive firing and membrane potential is oscillating. After that, the model is linearized and augmented with a washout filter to obtain a high pass filtered structure. Finally the projective control approach is utilized to produce a static output negative feedback on the washout filter output to finish the application. The simulation results show that the control laws successfully stabilized the bifurcating nerve fibers with a short lasting electric field exertion on the fiber. The disadvantage of the method itself is that it requires the bifurcating conditions to be known. If a parameter identification method is proposed for the Hodgkin – Huxley model by the measurement of the membrane potential for various types of nerve fibers. So if the model is properly identified, the research can be beginning point in the treatment of diseases based on repetitive firing. In the reverse direction, a stable fiber can be forced to repetitive firing condition by using approaches like this. For example, if the dendrite and soma membrane potentials can be separately measured a pair of pure complex conjugate eigenvalues can be placed so that the

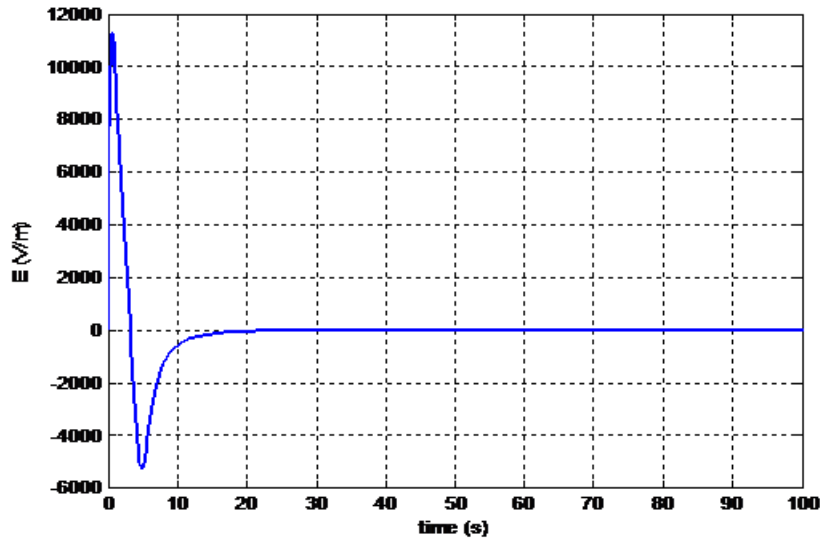


Figure 3.3: The required level of electric field for stabilizing the nerve fiber (only the first 100 seconds are shown where it stays at zero level after all)

system is forced into a Hopf bifurcation condition. This will be required since in both Hopf and saddle node bifurcations a pair of eigenvalue at the specified properties are required.

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